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Cryospray reduces pain during venous cannulation in elective surgery patients: a randomized placebo-controlled study

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Abstract

Background Venous cannulation is widely used in healthcare systems, and for many patients, it is painful and distressing. We hypothesized that the rapid onset of cryospray use would reduce pain from venous cannulation compared to the use of a placebo spray.

Methods The trial was a prospective randomized placebo-controlled trial including 130 adult patients scheduled for elective surgery. Patients were randomized to receive either cryospray or placebo before venous cannulation. The primary outcome was patient-reported pain from vein puncture.

Results There were no differences in the baseline variables between the two groups with respect to age, sex, height, weight or ASA class. Patients in the cryospray group indicated more pain or discomfort with the application of the spray (0 (0-2.5)) than with the application of the placebo spray (0 (0–0)) ($P < 0.005$), as measured by the Numeric Rating Scale (NRS). Patients in the placebo group reported more pain with vein puncture than did those in the cryospray group (1 (0–3) vs. 3 [2–5], $P < 0.005$). When asked if the patient would have the same spray in case of canulation again, 57 patients from the cryospray group reported yes compared to 34 patients in the control group ($P < 0.005$).

Conclusions This randomized study found that cryospray significantly reduced pain during venous cannulation without increasing procedure difficulty. Patients reported lower pain scores and a greater preference for cryospray in future procedures, supporting its use as an effective pain relief method in elective surgery.

Trial registration ClinicalTrials. gov Identifier: NCT04865783 (28-04-2021).

Keywords Vapocoolant, Topical anesthetics, Intravenous cannulation, Procedural pain, Pain relief

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Background

Venous cannulation is a common practice in the health care system. Before any procedure, intravenous access provided before the induction of anesthesia. For many patients, the placement of a venous catheter is associated with pain and discomfort. Any quick and easy reduction in pain during the procedure, not making intravenous access more difficult, would therefore be very important for most patients. Cryospray has been described as an easy-to-use supplement for analgesia to alleviate pain during intravenous access [1–3]. Furthermore, cryospraying should not increase the difficulty of intravenous cannulation [4]. Comparing cryospray to infiltration analgesia, the latter includes further painful injections for the patients and potential damage to the skin. This would make further canulation even more difficult. Cryospray has been reported to reduce pain during venous cannulation in the emergency setting or without any effect [1, 5] No trials have been published investigating the effect of cryospray in the elective setting. A search of the literature revealed 3 recent meta-analyses reporting conflicting findings [6–8]. All of these meta-analyses call for further research, especially on patient satisfaction. The fact that cryosprays are not widely used calls for further research in this area.

The purpose of the present trial was to evaluate whether cryospray can reduce pain from intravenous cannulation to elective surgery compared to placebo spray. By randomizing patients to either cryospray or placebo before venous cannulation, we hypothesized that cryospray reduces pain from venous cannulation compared to placebo without any difference in successful cannulation on the first attempt. The primary outcome was patient-reported pain from vein puncture.

Method

Study design and settings

The trial was a prospective randomized placebo-controlled trial. The trial was conducted at the general operating theater at Hospital Sønderjylland Southern Denmark.

Study participants

The inclusion criteria were patients scheduled for elective surgery with a need for an intravenous line, a minimum age of 18 years and who were able to give consent. The exclusion criteria included infection, coloring or bruising at the puncture site, no vein signs visible after the application of vein stasis, allergy to coolant spray, contraindication for vein stasis, vein cannulation, earlier participation in the trial or Raynards syndrome.

Procedure

Patients provided informed consent before enrollment in the trial. Patients were assigned to either cryospray or placebospray by randomization. Patients were blinded to whether a cryospray or placebo was used. The cryospray used was Chloraethyl spray cans “Dr. Henning” (Dr. Georg Friedrich Henning, Chemische Fabrik Walldorf GmbH, Robert-Bosch-Strasse 62, D-69190 Walldorf). The spray used for the control was an unbuffered saline solution, which was obtained from the hospital pharmacy “Apotekets Sårskyl” (Aurena Laboratories AB, Fjärrviksvägen 22, 65350 Karlstad, Sweden).

Two nurse anesthesia specialists performed the procedure, including information and consent. After consent was obtained, one person randomized and applied the spray. The other person was blinded to the randomized treatment and performed the vein puncture.

After application of vein stasis cryospray or saline was sprayed from a distance of 15–20 cm on the back of the patient’s hand. The spray was applied 2 times for 2 s at 2 s intervals. Within 30–45 s after application of the spray and disinfection, the person blinded to the randomized treatment placed the intravenous line. A standard 20G needle was used.

Data collection

The anesthesia nurse who performed the puncture but was blinded to the randomization was asked the following questions: could the veins be seen with vein stasis (yes/no), did the application of spray make it more difficult to see the vein (yes/no), and was the vein successfully cannulated in the first attempt (yes/no).

The patient was asked about pain or discomfort with the application of the spray (cryo- or placebo) but before vein puncture using the NRS (0–10, zero no pain and 10 very painful).

The patient was asked after successful placement of the intravenous line about pain from the puncture site (numeric rating scale (NRS)) and whether the patient would have the same spray in case of canulation again (yes/no).

After discharge from the recovery room, patients were asked for any discomfort or pain from the puncture site.

Statistics

An absolute reduction in the NRS score of 1.5 was considered clinically relevant. According to previous trials, an NRS score of 3.5 was expected in the noncryo-treated group [1]. With a risk of type I error of 0.05 and a power of 90%, a total of 116 patients were needed. To compensate for dropouts, we planned to enrol a total of 130 patients (65 patients in each group).

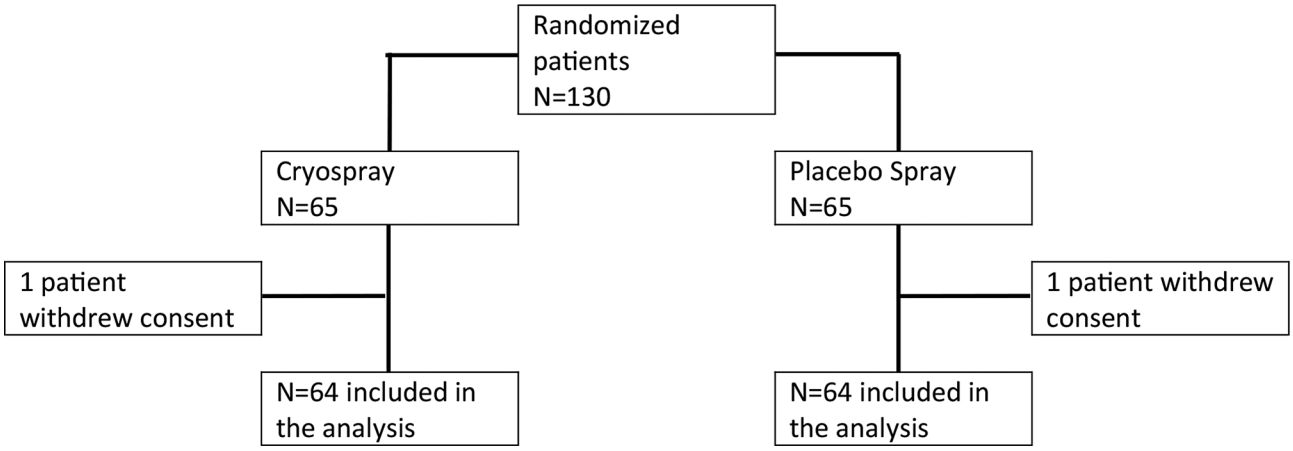

Fig. 1 Participant flow diagram

Table 1 Baseline data. All values are presented as medians (IQRs) or numbers (%)

Total number of patients (*N* = 128))	Cryospray group (*n* = 64)	Placebo group (*n* = 64)	*P* value
Age (years)	61 (52-69.5)	63.5 (56.5–71)	0.32
Gender			
Female	31 (48%)	29 (45%)	0.72
Male	33 (52%)	35 (55%)	
Height (cm)	175 (168–183)	173.5 (168–179)	0.41
Weight (kg)	80 (66.5–89)	80 (71–91)	0.37
ASA	2 (1–2)	2 (1–2)	0.23

Table 2 Results from nurses performing the procedure. All values are presented as medians (IQRs) or numbers (%)

Total number of patients (*N* = 128))	Cryospray group (*n* = 64)	Placebo group (*n* = 64)	*P* value
Visible veins before application of cryospray (with vein stasis)			
Yes	64 (100%)	63 (98%)	1.00
No	0 (0%)	1 (2%)	
Visible veins after application of cryospray (with vein stasis)			
Yes	64 (100%)	64 (100%)	N/A
No	0 (0%)	0 (0%)	
Successful vein cannulation in first attempt			
Yes	62 (97%)	58 (91%)	0.27
No	2 (3%)	6 (9%)	

Randomization was performed with sealed envelopes. The data were first written on a CRF paper. Afterwards, the data were entered into an access database.

The data were analyzed using the Wilcoxon rank-sum test and chi2 test, as appropriate. All tests were performed using Stata Statistical Software (StataCorp. 2023. Stata Statistical Software: Release 18. College Station, TX: StataCorp LLC).

Ethics

The trial was approved by the Scientific Ethics Committee for the Region of Southern Denmark (project ID: S-20210023, approved 10th of February 2021). Furthermore, the trial was recorded as a clinical trial at ClinicalTrials. gov (identifier: NCT04865783). Patients provided informed consent before enrollment in the trial. The study adheres to CONSORT guidelines.

Results

A total of 130 patients were randomized from 17th of June 2021 to 18th of July 2023. Two patients withdrew consent after randomization (one from each group) (Fig. 1). No differences were detected in the baseline variables (cryospray vs. placebospray) with respect to age (61 (52-69.5) vs. 63.5 (56.5–71), $P=0.32$), sex (female 24% vs. 22.5%, $P=0.72$), height in cm (175 (168–183) vs. 173.5 (168–179), $P=0.41$), weight in kg (80 (66.5–89) vs. 80 (71–91), $P=0.31$) or ASA class (2(1–2) vs. 2(1–2), $P=0.23$) (Table 1).

In both groups, most patients had visible veins before the application of cryospray (with vein stasis) (Table 2). All patients had visible veins after the application of cryospray (with vein stasis) (Table 2). Sixty-two patients in the cryospray group were successfully cannulated via veins on the first attempt, while 58 patients in the placebo group were successfully cannulated ($P=0.27$) (Table 2).

Patients in the cryospray group indicated more pain or discomfort with the application of the spray (0 (0-2.5)) than with the application of the placebo spray (0 (0–0)) ($P<0.005$), as measured by the NRS. Patients in the placebo group reported more pain with vein puncture than did those in the cryospray group (1 (0–3) vs. 3 [2–5], $P<0.005$). When asked if the patient would have the same spray in case of canulation again, 57 patients from the cryospray group reported yes compared to 34 patients in the control group ($P<0.005$) (Table 3).

Table 3 Patient results. All values are presented as medians (IQRs) or numbers (%)

Total number of patients (*N* = 128))	Cryospray group (*n* = 64)	Placebo group (*n* = 64)	*P* value
Pain or discomfort with application of the spray (cryo- or placebo) but before vein puncture. Numeric Rating Scale (zero no pain and 10 very painful)	0 (0-2.5)	0 (0–0)	< 0.005
Pain from the puncture site (Numeric Rating Scale) during vein puncture	1 (0–3)	3 (2–5)	< 0.005
Would the patient have the same spray in case of canulation again in the future			
Yes	57 (89%)	34 (53%)	< 0.005
No	7 (11%)	30 (47%)	

One patient from the control group reported pain or discomfort from the puncture site when asked in the post anesthesia care unit, but this was within what was expected (data not shown). No other patients from either group reported any pain or discomfort from the puncture site in the post anesthesia care unit (data not shown).

Discussion

In this trial, we reported that cryospray is easy to use without making "first-time vein cannulation" more difficult. Furthermore, patients who received a cryospray reported less pain during vein cannulation, and more patients preferred the same spray in future canulations than did patients who received a placebo spray.

Measures to alleviate pain from vein puncture should be easy to use, avoid making vein cannulation more difficult and cause very low discomfort for patients. Other measures, such as topical application of local anesthetics, are time dependent and should be applied at least one hour before cannulation. Furthermore, this approach has a very specific area of effect, which might be a problem because of the need to change the puncture site. Furthermore, there is a risk of making vein cannulation slightly more difficult. Infiltration analgesia is another way to provide analgesia before elective vein puncture. However, there is a risk of one or more skin punctures beside the actual vein puncture. This approach also carries the risk of making vein puncture more difficult.

Mace randomized patients in the emergency department [1]. Including acutely admitted patients at risk of pain from sites other than the puncture site might influence patients' reports of pain. Furthermore, vein cannulation could be difficult for other reasons in the acute setting (hypovolemia, hypothermia, pain, etc.) This is less likely in the elective setting. In the former trial, the spray was applied for 4 to 10 s. Testing with coolant spray in our unit before initiating the trial showed that it was painful to apply the coolant spray for more than 2 s. Therefore, we chose to apply the spray 2 times in two seconds with a 2 s break between the two applications. This approach was shown to be a feasible and safe compromise with very low discomfort for the patient and to not make vein cannulation more difficult.

Several limitations should be considered. As mentioned above, only elective adult patients with an ASA score of 1–2 were included. Therefore, the results from this trial cannot necessarily be generalized to acutely admitted patients, children or patients with an ASA class > 2. Furthermore, the nurse specialists who randomized and performed the vein cannulation were all well experienced in the procedure. The results therefore do not state anything about the effect of cryospray applied with less experienced personnel.

Furthermore, although the setup was blinded one cannot rule out that a healthcare person with experience in vein cannulation could tell the difference between the use of a saline spray and a cryospray when performing the vein cannulation. However, this is not reflected in the report from vein cannulation. Since both groups had 100% visible veins before the procedure (Table 2).

Conclusion

This randomized placebo-controlled trial demonstrates that cryospray effectively reduces pain during venous cannulation without complicating the procedure. Patients preferred cryospray over placebo for future use. While the study focused on elective adult patients, further research is needed to evaluate its use in other patient populations.

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Author contributions

JBP, AM PF, SA, RP and TS conceived and developed the protocol. JBP, AM and TS applied for ethical and data protection permission. JBP, AM and TS developed the database. JBP and AM screened, included, randomized and performed the procedures. JBP, AM PF, SA, RP and TS analyzed the data. JBP, AM PF, SA, RP and TS wrote the manuscript. All authors have approved the final version of the manuscript.

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Data availability
Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The trial was approved by the Scientific Ethics Committee for the Region of Southern Denmark (project ID: S-20210023). All participants gave full informed consent before enrollment in the trial. Furthermore, the trial was recorded as a clinical trial at ClinicalTrials. gov (identifier: NCT04865783). The study adheres to CONSORT guidelines.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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